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***A review of bovine fasciolosis and other trematode infections in
Nigeria***

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Abstract

Trematode infections cause serious economic losses to livestock worldwide. Global production losses due to fasciolosis alone exceed US\$3 billion annually. Many trematode infections are also zoonotic and thus a public health concern. The World Health Organisation has estimated that about 56 million people worldwide are infected by at least one zoonotic trematode species and up to 750 million people at risk of infection. Fasciolosis caused by the fluke, *Fasciola gigantica* is endemic in Nigeria and is one of the most common causes of liver condemnation in abattoirs. Cattle total losses from *Fasciola* infection in Nigeria have been estimated to cost £32.5 million. Other trematode infections of cattle including paramphistomosis, dicrocoeliasis and schistosomiasis have all been reported in various parts of Nigeria with varying prevalence.

Most publications on trematode infections are limited to Nigerian local and national journals with very few international. This paper therefore summarised the current data on distribution, control and zoonotic trematode infections in Nigeria and other African countries. We also identified research gaps and made recommendations for future research and areas for funding for policy/planning.

Introduction

Nigeria is one of the four leading livestock producers in Sub - Saharan Africa (FAO, 2009) contributing up to 12.7% of the total Nigerian agricultural gross domestic products (CBN, 1999). In the tropics, cattle are generally reared under the transhumance husbandry systems with little supplementary feeding resulting in low productivity and high pre-weaning mortality (Ulayi *et al.*, 2007). Also, acute shortage of feeds during the dry season remains a common occurrence, compelling these animals to graze around water bodies that are often heavily infested with potential intermediate hosts of trematode infections (Ulayi *et al.*, 2007).

Trematode infections of cattle including fasciolosis (Babalola & Schillhorn van Veen, 1976, Dipeolu *et al.*, 2000), paramphistomosis (Bogatko, 1975), dicrocoeliasis (Schillhorn van Veen *et al.*, 1980, Ulayi *et al.*, 2007) and schistosomiasis (Pugh *et al.*, 1980, Ndifon *et al.*, 1988) have all been reported in various parts of Nigeria. They are referred to as 'digenetic' because they require at least two different kinds of hosts for their full development. The first are the intermediate hosts of mollusc species (slug, snail or shell fish) while the final hosts are vertebrates (Taylor, 1964). Mixed infection with more than one trematode species is a common occurrence in animals due to similarities in life cycles. *Fasciola* infection has been reported to occur concurrently with *Schistosoma* and paramphistome species (Schillhorn van Veen *et al.*, 1980, Yabe *et al.*, 2008). It is also reported to occur concurrently with *Dicrocoelium* species (Schillhorn van Veen *et al.*, 1980, Ulayi *et al.*, 2007). Infection with trematode parasites can lead to severe losses to farmers hence affecting sustainability of food production (Alvarez Rojas *et al.*, 2014).

Fasciolosis, which is also referred to as distomatosis or liver fluke disease, is a parasitic disease caused by the trematode of the genus *Fasciola*. The most important species are *F. hepatica* and *F. gigantica*, found in the temperate and tropical regions of the world respectively. The geographical distribution of *Fasciola* species is determined by the distribution of the snail intermediate hosts (Boray, 1985). The temperate disease occurs in Europe, America and Oceania while the tropical fasciolosis is common in Africa, Indian sub-continent, Central

and Southeast Asia and other subtropical and tropical areas of the world (FAO, 1993). Both species overlap in many areas of Africa and Asia (Walker *et al.*, 2008). Adults of each species can occur concurrently in the same animal host, either because of local overlap or because of livestock movement (Mas-Coma *et al.*, 2009). The two *Fasciola* species may hence interbreed resulting in hybrids species (Agatsuma *et al.*, 2000, Ashrafi *et al.*, 2006). They are hermaphrodites and are found in the bile ducts of a large number of herbivorous ruminants, equine, pigs, rabbits (FAO, 1993) and wild animals (Hammond, 1972). Man is also a suitable host (Boray, 1969). The intermediate hosts of *F.gigantica* are true water snails belonging to the phylum *Mollusca*, class *Gastropoda* and subclass *Pulmonata* (Wright, 1971). They belong to the family *Lymnaeidae* and super species *Lymnaea (Radix) auricularia sensu lato*.

Paramphistomes Fiscoeder 1901 also known as rumen flukes are gastro-intestinal trematodes belonging to the family of *Paramphistomatidae* (Soulsby, 1982). These are conically shaped flukes measuring 5-12 mm × 2-4 mm. The adults predilection sites are the rumen and reticulum of ruminants while the immature parasites are found in the small intestines and abomasums (Rojo-Vázquez *et al.*, 2012). Snails of the families *Planorbidae*, *Bulinidae* and *Lymnaeidae* act as intermediate hosts (Soulsby, 1982, Castro-Trejo *et al.*, 1990). They are largely non-pathogenic but clinical outbreaks have been reported to occur. The most important species in Africa is *Paramphistomum microbothrium* (Dinnik, 1964). Others are: *P. cervi* (European Environment), *P. ichikawar* (Australasia) (FAO, 1993) and *P. daubneyi* first described in Kenya and common in Europe (Abrous *et al.*, 1996). Recently there are reports of increasing number of cases of rumen flukes identified mainly as *Calicophoron daubneyi* in cattle and sheep in the republic of Ireland (Zintl *et al.*, 2014, Toolan *et al.*, 2015). The adult paramphistomes are regarded as commensals in the rumen as heavy infections are tolerated without causing any damage to the rumen (Dinnik, 1964) although immature parasites in the small intestine cause clinical disease (Aiello, 1998).

Dicrocoelium species, commonly referred to as the lancet fluke, are found in the bile duct of domestic and wild ruminants (Otranto & Traversa, 2002, Taylor *et al.*, 2007). Other animals such as rabbits, pigs, dogs, horses and human can also be

infected (Rojo-Vázquez *et al.*, 2012). There are several species; with *D. dendriticum* (Otranto *et al.*, 2007) having the widest distribution worldwide while *D. hospes* is common in Africa (Aiello, 1998). Other species are *D. chinensis* and *D. suppereri* (Rojo-Vázquez *et al.*, 2012). Two intermediate hosts are required. The first intermediate host is a terrestrial snail of the genus *Limicolaria* while the second intermediate hosts which are brown ants of the genus *Formica* (Soulsby, 1982).

Schistosoma species are elongate, unisexual trematodes commonly referred to as blood flukes and widely distributed throughout Africa, Middle East, Asia and some Mediterranean countries (Soulsby, 1982). They are found in the blood vessels such as portal, mesenteric and intestinal veins of domestic animals (Aiello, 1998). The species, *Schistosoma matteei* and *S. bovis* are common in Africa, Middle East and southern Europe (Vercruysse & Gabriel, 2005, Taylor *et al.*, 2007). *S. bovis* are the most pathogenic in animals in Africa (Vercruysse & Gabriel, 2005). They occur in the portal and mesenteric vessels of cattle, sheep and goats. They are similar to the human parasite *S. haematobium* (Soulsby, 1982). *S. matteei* has also been reported in sporadic human infection. Other African species in ruminants includes *S. curassoni* (common in Western Africa), *S. margreboweiei* and *S. leiperi*. In Asia, *S. spindale*, *S. nasale* (nasal worm), *S. indicum*, *S. incognitum* and *S. japonicum* (which are zoonotic in Far East) (De Bont & Vercruysse, 1997). Aquatic snails such as *Bulinus*, *Physopsis*, *Oncomelania*, *Lymnaea* and *Indoplanorbis* act as the intermediate hosts (Taylor, 2007).

This review aims at describing the current status of bovine fasciolosis and other trematode infections in Nigeria and surrounding African countries, in relation to economic losses, distribution, molecular studies, control strategies and human infections. Data were collected from publications obtained from online search as well as local national journals. Bovine fasciolosis is reported in literatures across different states of Nigeria were mapped by using QGIS® software v2.12 (Lyon, France).

Economic losses from trematode infections

Tropical fasciolosis caused by *Fasciola gigantica* is regarded as one of the most important single helminth infection of ruminants in Asia and Africa (Boray, 1985, Fabiyi, 1987). Economic losses from fasciolosis are often difficult to estimate and may result directly from increased liver condemnation or indirectly from decreased livestock productivity (Taylor, 1964). Although direct losses are easier to measure, indirect losses are considered to be far more economically important (Kaplan, 2001). With the total cattle population in Africa estimated at 201 million animals, an annual loss of about US\$840 million from fasciolosis infection is predicted (Spithill *et al.*, 1999), but this cost is likely to have increased significantly in the last eighteen years. Production losses in liver fluke infected cattle often take the form of reduced milk production in dairy cattle and poor feed conversion in beef cattle (Armstrong, 1982). A linear relationship between burden of adult *F. gigantica* and weight gain of cattle has been described, with infected animals gaining only about half the annual weight compared to control (Sewell, 1966). The amount of weight loss may also, however, be dependent on age, level of nutrition and intensity of infection (Spithill *et al.*, 1999). Other clinical manifestations are anaemia, reduced fertility and reduced work capacity (Hillyer, 2005), and where there is massive infection with immature parasites, sudden death could occur and lead to serious economic losses (Torgerson & Claxton, 1999, Rojo-Vázquez *et al.*, 2012).

Severe infection with immature paramphistomes can cause great economic losses due from reduced weight gain and decrease in milk production (Horak, 1971). Paramphistomosis has been reported to cause between 30-40% mortality in cattle and sheep. These deaths may result from anaemia, hypo-proteinaemia, profuse diarrhoea and marked emaciation (Soulsby, 1982), and a decrease in milk yield in dairy cattle (Spence *et al.*, 1996).

Economic losses from dicrocoeliasis is less apparent compared to those from other trematode infections and is difficult to quantify due to concurrent infection with other gastrointestinal parasites. This may also be largely due to the asymptomatic nature of the disease (Otranto & Traversa, 2003). Clinical signs are mostly absent

but losses occur mainly from liver condemnation due to fibrosis of bile ducts and cirrhosis (Taylor, 2007).

An abattoir survey to determine the prevalence and species of cattle schistosomiasis in Zambia revealed an overall prevalence of 51%, with 93% of the infected animals having up to 100 worm pairs in the mesenteric veins; *Schistosoma mattheei* was the predominant species (75%); while *S. leiperi* (12%) and *S. margrebowiei* (2%) were also reported (De Bont *et al.*, 1994). Schistosomiasis due to *Schistosoma bovis* has also been reported with a prevalence rate of 4.8% in Tanzania (Nzalawahe *et al.*, 2015). These parasites cause economic losses due to their long-term effect on growth and productivity and also due to increased susceptibility to other parasitic and bacterial diseases (De Bont & Vercruysse, 1998). The clinical signs associated with the intestinal and hepatic form of disease in ruminants are haemorrhagic enteritis, haematuria, anaemia and loss of weight with death within few months of the disease. Nasal schistosomiasis, on the other hand, is a chronic disease that causes coryza and dyspnea in infected animals (Aiello, 1998). Production losses reported due to schistosomiasis in cattle are attributed mainly to losses occurring in animals aged between 6-30 months and are due to reduced weight gain, liver condemnation, poor future reproductive performance and death (Hunt *et al.*, 1984). Also approximately 165 million cattle are likely to be infected with *Schistosoma* species worldwide (De Bont *et al.*, 1994).

Many trematode infections are also zoonotic and thus a public health concern (Chen & Mott, 1990, Mas-Coma *et al.*, 2005, Wolfe, 1966). The World Health Organisation has estimated that about 56 million people worldwide are infected by at least one zoonotic trematode species (Furst *et al.*, 2012) and up to 750 million people at risk of infection (Keiser & Utzinger, 2009). It has been suggested that recent environmental changes associated with global warming which favours the development of snail intermediate hosts contribute to an increase in disease outbreaks (Mitchell, 2002).

Epidemiology of bovine fasciolosis in Nigeria

Tropical fasciolosis due to *F. gigantica* Cobbold 1855 has been reported in several parts of Africa (Schillhorn van Veen, 1980, Phiri *et al.*, 2005a, Abebe *et al.*, 2010, Nzalawahe *et al.*, 2014) and is likely to be a problem throughout the continent. The two species of *Fasciola*: *F. gigantica* and *F. hepatica* and their respective snail intermediate hosts have both been reported in Africa. Fasciolosis is endemic in Nigeria and is of great economic importance (Ogunrinade & Ogunrinade, 1980). The disease has been reported with varying prevalence across the country and is one of the most common causes of liver condemnation in abattoirs. The prevalence distribution of bovine fasciolosis is mapped (fig 1) according to available data published between 1980 and 2016 (Schillhorn van Veen, 1980, Nwosu & Srivastava, 1993, Nkwu *et al.*, 2004, Opara, 2005, Ekwunife, 2006, Adedokun *et al.*, 2008, Umar *et al.*, 2009, Ibironke & Fasina, 2010, Sugun *et al.*, 2010, Omoleye, 2012, Gboeloh, 2012, Odigie & Odigie, 2013, Abraham, 2014, Ardo, 2014, Magaji, 2014, Ngele & Ibe, 2014, Yahaya & Tyav, 2014, Onyeabor, 2014, Ejeh *et al.*, 2015, Elelu *et al.*, 2016). The high prevalence rate from liver condemnation in a 3-year period reported in Lagos State (Ibironke & Fasina, 2010) can be explained by the fact that Lagos State is the commercial nerve centre of Nigeria with a very large human population, large number of cattle from all over the country are often slaughtered from the abattoir.

Cattle total losses from *Fasciola* infection alone in Nigeria have been estimated to cost £32.5 million (Fabiya & Adeleye, 1982). A survey of abattoirs in Nigeria showed that about 70% of organ condemnation, mainly of livers was due to fasciolosis (Alonge & Fasanmi, 1979). A recent study reported up to 88.1% liver condemnation due to liver flukes alone in Lagos abattoir (Ibironke & Fasina, 2010). These studies are in agreement with a 3-year abattoir study in South-western Nigeria in which losses from liver condemnation were estimated at US\$134,000 (Ibironke & Fasina, 2010). These data translate to huge economic losses from cumulative condemnation across the country.

Acute fasciolosis due to the migration of juvenile flukes is rare in cattle; however, a few cases have been reported in Nigeria. For example, on a dairy farm in North-central Nigeria, a pregnant cow was reported to have died during parturition,

where post mortem examination revealed inflammatory lesion and fibrosis due to fasciolosis (Okaiyeto *et al.*, 2012). The chronic form of the disease is the most common in cattle in Nigeria (Ogunrinade & Adegoke, 1982) and it occurs when small numbers of flukes finally enter the bile duct and infection becomes patent. This results in a chronic wasting disease from slow acquisition of liver flukes for months or even years. The normal tissues of the liver are replaced by fibrous tissues, with hyperplastic cholangitis and macroscopically visible calcification of the bile ducts giving rise to so called 'pipe-stem liver' (Taylor *et al.*, 2007; Soulsby, 1982). Clinically, the condition is characterised by weight loss, anaemia, and oedema at the jaw (bottle jaw), thoracic and lower abdominal regions (Radostits *et al.*, 2000, Mitchell, 2002, Taylor *et al.*, 2007, Rojo-Vázquez *et al.*, 2012).

Factors influencing outbreak of bovine fasciolosis

Season of the year

There are varying reports on the seasonal infection rates of *F. gigantica* across Nigeria. Majority of studies reported high infection rates in the beginning of the dry season (Schillhorn van Veen *et al.*, 1980, Umar *et al.*, 2009) which is in agreement with studies in other parts of Africa like Zambia, where bovine fasciolosis was also reported with higher fluke abundance reported in the post-rainy season (Phiri *et al.*, 2005b). Similar observations were made in Zimbabwe, where *Fasciola* faecal egg counts were reported to follow a seasonal variation with increase during end of dry season with highest liver condemnation reported during the rainy season (reviewed by Pfukenyi *et al.*, 2005). However, another study carried out in the Southern part of Nigeria reported an all year occurrence of infection (Gboeloh, 2012). This all year occurrence in the South was attributed to the favourable climatic condition (warm and humid) which favours development of parasites, and the increase in the density of snail intermediate hosts (Gboeloh, 2012). The climatic condition in Southern Nigeria could be likened to those of highland areas of Iringa, Tanzania (Nzalawahe *et al.*, 2015) and Zimbabwe (Pfukenyi *et al.*, 2006a) where wet/swampy grazing areas reportedly favour availability and distribution of snail intermediate host. In addition a recent study in Tanzania have associated trematode infections including *Fasciola* with irrigation practices during the dry season that favours growth of intermediate snails hosts and development of trematode larval stages (Nzalawahe *et al.*, 2014).

Type of management system

The type of management system has been shown to significantly influence the prevalence of *Fasciola* infection (Keyyu *et al.*, 2005). A low prevalence rate was also reported to occur in cattle reared by sedentary husbandry system in Lake Chad area (Jean-Richard *et al.*, 2014). While a high prevalence rate of 54.3% has been reported in cattle managed extensively in South western Nigeria (Adediran *et al.*, 2014), this is not surprising because, cattle come into contact with snail-infected habitat during extensive communal grazing. In contrast, under intensive management systems, metacercaria-free water and herbage can be supplied to the cattle thereby minimizing the likelihood of outbreaks of fasciolosis.

Age of cattle

In a recent study from Nigeria, *F. gigantica* infection was reported to be higher in adult cattle than weaners (Elelu *et al.*, 2016). This is in agreement with past studies in Africa with similar findings (Pfukenyi *et al.*, 2006a, Nzalawahe *et al.*, 2014). The difference in prevalence within age group was attributed to longer length of exposure to the infection in adults compared to weaners (Pfukenyi *et al.*, 2005, Nzalawahe *et al.*, 2014). It was also concluded that adult cattle act as a constant source of *F. gigantica* infection for the more susceptible young animals (Pfukenyi *et al.*, 2005).

Distribution of snail intermediate host

The intermediate snail host *Lymnaea (Radix) natalensis* that is widespread throughout Africa is also widely distributed in Nigeria, although its occurrence is restricted to permanent water bodies (Ndifon & Ukoli, 1989). *Lymnaea* is fairly common in regions with rainfall over 1000mm (Schillhorn van Veen, 1980) and it tolerates relatively high temperatures (Njoku-Tony, 2011) consistent with tropical climates. In Uganda, *L. (Radix) natalensis*, the intermediate snail host of *F. gigantica*, is the vector commonly found abundant at lower altitudes below 1800m, while *Galba truncatula* (intermediate snail host of *F. hepatica*) was found only at altitudes above 3000m (Howell *et al.*, 2012). The presence of the two

vectors indicates the possibility of the two *Fasciola* parasites in Uganda. Other countries of Africa have however reported the presence of the two species of *Fasciola* (Yilma & Mesfin, 2000, Walker et al, 2008; Sisay & Nibret, 2013). To date the authors of this review are not aware of any report of *Galba truncatula* in Nigeria, although specific studies to identify these species in areas of high altitude might be worthwhile.

In Nigeria, during the wet season, many of the developing *Lymnaea* snails are washed away in torrential streams after heavy rain and this may be important in the spread of *Fasciola* (Schillhorn van Veen, 1980). Snails were also reported to be more abundant during the beginning of dry season, reach a climax in the middle of the dry season, but decrease towards the end of the dry season when most streams and pools dry up (Schillhorn van Veen, 1980). This is supported by a field study in south-western Nigeria which shows that dry season conditions favour snails and this was said to be due to low turbidity, reduced currents and substantial growths of algae and macrophytes (Ndifon & Ukoli, 1989). In the sub-tropical and tropical countries with distinct wet and dry seasons, optimal development of fluke eggs to miracidia occurs at the start of the wet season and development within the snail is complete by the end of rains (Taylor, 2007). The dry season therefore coincides with the snail shedding of cercaria and more animals grazing closer to streams and ponds thereby predisposing them to infection. Herdsmen migrate in search of water and grazing during the dry season and thousands of cattle often converge on the few ponds, which fail to dry up (Ikeme & Obioha, 1973).

Diagnosis of bovine fasciolosis

The most common method of diagnosis is by faecal egg counts and pathological lesions in the liver during abattoir examination. Serological diagnostic method to detect antibodies, such as indirect ELISA (Damwesh & Ardo, 2013, Aliyu *et al.*, 2014) and direct ELISA (Fagbemi *et al.*, 1997) has been carried out in Nigeria. Another method of diagnosis is testing for precipitating antibodies using the Agar Gel Precipitation Test (AGPT) (Adedokun *et al.*, 2008). Comparatively, this method has been shown to detect more positive cases than faecal and bile egg counts (Adedokun *et al.*, 2008). In Kwara State, North-central Nigeria, survey of

cattle for fasciolosis revealed a higher prevalence rates from faecal analysis compared to a previous abattoir study that utilized liver examination. This further showed the lack of sensitivity of the abattoir method of diagnosis as positive samples are likely to be lost (Elelu *et al.*, 2016).

Epidemiology bovine paramphistomosis in Nigeria

Rumen flukes are paramphistome parasites commonly seen in the abattoir in Nigeria (Bunza *et al.*, 2008). The snail vector of the disease (*Lymnaea*, *Planorbis* and *Bulinus*) has also been reported in Nigeria (Ndifon & Ukoli, 1989, Brown & Kristensen, 1993). The species reported to occur in Nigerian domestic livestock include *Paramphistomum microbothrium*, *Carmyerius gregarius*, *Carmyerius spatiosus* *Cotylophorum cotylophorum* (Schillhorn van Veen *et al.*, 1975) and *Paramphistomum cervi* (Bogatko, 1975). Others species recovered from Nigerian cattle are *Ceylonocotyle dicranocoelium*, *Bothriophoron bothriophoron*, *Calicophoron calicophorum* and *Calicophoron microbothrioides* (Dube *et al.*, 2013).

Prevalence rates of 2.2% (Edosomwan & Shoyemi, 2012); 18.8% (Nwigwe *et al.*, 2013); 16.1% (Elelu *et al.*, 2016) has been reported for paramphistomes in past studies in Nigeria. A higher prevalence rate of 41.67% for *P. cervi* was reported in another abattoir study in Northern Nigeria (Nnabuike *et al.*, 2013). Similarly, also in Northern Nigeria a high paramphistome prevalence rate of up to 56.0% in slaughtered cattle has been reported in a study area around a marshy river valley. The grazing land associated with this river valley provides suitable breeding sites for snail intermediate hosts of the parasites (Bunza *et al.*, 2013). The convergence of cattle in common graze land during dry season as well as irrigation practices has been implicated in high prevalence of paramphistomosis (Nzalawahe *et al.*, 2014). In a cross-sectional study in Ethiopia, 51.8% of cattle slaughtered were positive for paramphistomosis with peak prevalence rates observed during October to November (Ayalew *et al.*, 2016). Although adult cattle were more likely to be infected with paramphistomes because they are more likely to be infected when taken out for grazing, however several studies have shown that there is no statistically significant difference in paramphistome infection between age groups of cattle (Titi *et al.*, 2010, Tadesse *et al.*, 2014, Khedri *et al.*, 2015, Ayalew *et al.*, 2016).

Epidemiology of bovine dicrocoeliasis in Nigeria

There are records of *Dicrocoelium hospes* infection in cattle in Nigeria (Nwosu & Srivastava, 1993, Ulayi *et al.*, 2007), and snail species of *Limicolaria flammea* have been experimentally shown to be a suitable intermediate host of the disease (Fashuyi & Adeoye, 1986). The majority of prevalence data are based on abattoir surveys (FAO, 1992). Studies carried out in Zaria abattoir, Northern Nigeria recorded high prevalence rates of 56.0% (Schillhorn van Veen *et al.*, 1980) and 35.4% (Ulayi *et al.*, 2007) from cattle for *D. hospes*. A low prevalence rate of 18.3% in Borno State (Nwosu & Srivastava, 1993), and 22.33% was also reported in Plateau State in bile duct of cattle (Omowaye *et al.*, 2012). Seasonal infection rates have also been reported for of *D. hospes* in Nigeria, with highest rate occurring during and directly after the rainy season (Schillhorn van Veen *et al.*, 1980).

Epidemiology of bovine schistosomiasis in Nigeria

Schistosoma curassoni and *S. bovis* have been reported in cattle in Nigeria (Ndifon *et al.*, 1988, Elelu *et al.*, 2016). The intermediate snail host (*Bulinus globosus*) of *Schistosoma* species is present in Nigeria (Ndifon and Ukoli, 1989) and has been successfully experimentally infected with *S. bovis* miracidia originating from a Nigerian cow (Ndifon *et al.*, 1988). The transmission of *S. mattheei* has been reported with an all year round occurrence with high prevalence during the wet months (Pfukenyi *et al.*, 2005). The prevalence rates reported in Nigeria were 7.8% for *S. bovis* and 2.2% for *S. curassoni* based on examination of rectal scrapings, however a higher prevalence of 31.1% (including both species of *Schistosoma*) was observed in 502 slaughtered cattle by examination of mesenteric and rectal veins (Ndifon *et al.*, 1988). In another study that utilised a more sensitive ELISA technique, a higher prevalence rate (16.2%) was recorded in cattle of the Kuri breed compared with other breeds (Hambali *et al.*, 2016). This is not surprising as these breed of cattle with their characteristic bulbous horns are adapted to swimming, they are therefore more likely to come in contact with *Schistosoma* infected water. Schistosomiasis is transmitted via active skin penetration during contact with water. Other studies carried out in parts of North-Western Ethiopia located close to swampy areas reported higher prevalence rates

up to 24% in cattle (Lulie & Guadu, 2014). In addition, significantly higher schistosomiasis prevalence was observed in the wet season compared to the dry season in cattle in Zimbabwe (Pfukenyi *et al.*, 2006b). Higher prevalence rate (25.2%) has also been reported in cattle managed extensively compared to those under a semi-intensive management system (15.38%) (Lulie & Guadu, 2014).

Molecular identification of trematode species

Several PCR-based techniques have been used to identify digenetic trematodes (Lotfy *et al.*, 2008, Lotfy *et al.*, 2010). Molecular identification has an important contribution to make in many areas where there are problems associated with definitive speciation. These areas include instances of species overlap as seen in *Fasciola* (Kendall, 1965), the existence of hybrids between different genotypes (for example, the Japanese triploid forms (Itagaki & Tsutsumi, 1998), the identification of sexually immature paramphistome species (Horak, 1971), and difficulty in speciation based on morphology of parasite eggs (Itagaki *et al.*, 2003). Other reasons for molecular identification are the close relatedness between taxa as seen between *S. haematobium* and *S. bovis* (human and animal parasites) as well as difficulty in cercarial identification (Webster *et al.*, 2010).

Molecular studies by analysis of the first (ITS1) and second (ITS2) internally transcribed spacer of the ribosomal rDNA and the mitochondrial cytochrome c oxidase I (COI) gene has been carried out for *Fasciola* (Mas-Coma *et al.*, 2005, Ali *et al.*, 2008, Amor *et al.*, 2011, Amer *et al.*, 2011), paramphistome (Lotfy *et al.*, 2010) and *Dicrocoelium* (Otranto *et al.*, 2007). The ITS-1 and ITS-2 are highly conserved and useful for differentiating closely related taxa that have diverged relatively recently (<50 million years ago) (Mas-Coma & Bargues, 2009). The mitochondrial NADH dehydrogenase subunit 1 and COI were recently used to characterize *F. gigantica* from Nigeria (Ichikawa-Seki *et al.*, 2017). However further molecular studies from different parts of Nigeria is recommended in order to understand these important pathogens.

Other genetic methods such as the use of restriction fragment length polymorphism (PCR-RFLP) of ribosomal or mitochondrial genes using common

restriction enzymes (such as *AvaII* and *DraII*) have been used to analyse the whole of mitochondrial DNA to distinguish *Fasciola* species (Marcilla *et al.*, 2002), to identify species of paramphistomes (Itagaki *et al.*, 2003), to study genetic variability of *Dicrocoelium* species (Sandoval *et al.*, 1999), and also to distinguish between *S. haematobium* and *S. bovis* (Barber *et al.*, 2000, Webster *et al.*, 2010).

A polymerase chain reaction technique (PCR) has also been used to detect the *F. gigantica* infection status of snail intermediate hosts (Velusamy *et al.*, 2004, Kaset *et al.*, 2010). PCR technique used to amplify specific fragments of mitochondrial DNA in faecal samples in sheep has shown promise in early detection of *F. hepatica* infection (Martínez-Pérez *et al.*, 2012). Molecular identification of paramphistome species from Asia and elsewhere in Africa has been carried out (Lotfy *et al.*, 2010), however at time of writing this review, there are no records of such studies having been carried out in Nigeria. However, PCR to amplify species-specific genes has been used in differentiating human species of *Schistosoma* in Nigeria (Akinwale *et al.*, 2014) and also to identify *S. bovis* in Kenya (Kamanja *et al.*, 2011).

Control strategies for trematode infections

The principles behind the control of trematode infections are similar for all species (FAO, 1993). Conventional methods for control include strategic anthelmintic treatment to reduce environmental contamination, (FAO, 1993), snail eradication by use of molluscicides and improved drainage systems to adversely influence the snail habitats (Armour, 1975, De Bont & Vercruysse, 1997). The current control of *F. hepatica* in cattle in temperate regions where the disease is prevalent is often based on strategically timed flukicide treatment, which is determined by studying the seasonal transmission dynamics in numerous locations throughout the world (Kaplan, 2001). The tropical trematode infection caused by *F. gigantica* may be less amenable to this approach because the intermediate hosts *L. (Radix) natalensis* are true water snails (Sewell, 1966) and cattle can come into contact with infected snails while grazing around water bodies all year round. Control of *Dicrocoelium* infection is more difficult due to the complex life cycle involving terrestrial intermediate hosts. Control is therefore based on

chemotherapy and husbandry practices (avoiding grazing during early morning and late evening to avoid infective ants) (Otranto & Traversa, 2002).

Strategic chemotherapy

Strategic anthelmintic treatment based on epidemiological and meteorological data is important for the control of flukes (FAO, 1993). There are several drugs for the treatment of fasciolosis. These include: halogenated phenol (niclofolan, bithionol, hexachlorophene and nitroxynil); salicylanides (rafoxanide, oxyclozanide and closantel), benzimidazoles (triclabendazole and albendazole); sulphonamides (clorsulon), phenoxyalkanes (diamphenethides) (Fairweather & Boray, 1999a). Triclabendazole has been the preferred drug for treating liver fluke since 1983 due to its high efficacy against early immature, immature and adult flukes (Boray *et al.*, 1983). These drugs differ in their effectiveness against adults and immature flukes. Strategic antihelminthic use at 12-13 week intervals is effective against both mature and immature flukes and reduces intensity of infection over time. Seasonal occurrence of fasciolosis and suggestions for strategic antihelminthic treatments has been suggested of which in the tropics with fasciolosis outbreak all year round, treatment up to 4 times per year is recommended (Torgerson & Claxton, 1999). In Nigeria, some parts have reported seasonal trends in fasciolosis while some Southern parts of the country have reported an all year round occurrence (Gboeloh, 2012). Some authorities recommend that cattle should be dewormed regularly (Aliyu *et al.*, 2014), while others recommend treatment upon onset of clinical fasciolosis. Damwesh and Ardo (2015) proposed 2-3 annual treatments: at the start of the rainy season, mid rainy season and at the start of the dry season.

The anthelmintic drugs currently in use in Nigeria include: albendazole, nitroxynil, closulon and levamisole. However, a search in available literatures revealed that the preferred drug of choice against *Fasciola* (triclabendazole) is currently not available for use in Nigeria.

Neither triclabendazole nor niclofolan have been found to be effective against *Dicrocoelium* and paramphistome species (Güralp & Tina, 1984). The drugs of choice for paramphistome infection are resorantel, oxyclozanide and the combination of bithional and levamisole (Aiello, 1998). A combination of

oxyclozanide and levamisole is most effective against paramphistomosis in cattle given in two treatments 3 days apart (Rolfe & Boray, 1987). Strategic treatment during the dry season may reduce contamination of snail habitat in the following raining season (Rolfe *et al.*, 1991).

Benzimidazoles (except triclabendazole) and pro-benzimidazoles (thiophanate, netobimin) at higher doses are effective against *Dicrocoelium* species (Otranto & Traversa, 2002). Praziquantel is highly effective against all bovine visceral schistosomiasis (De Bont & Vercruysse, 1997) but is advised only in severe outbreaks due to the risk of portal occlusion from heavy worm burdens (McCully & Kruger, 1969). A combination of praziquantel and artemether is also effective against mature and immature schistosomes (Pfunkenyi *et al.*, 2005).

Anthelmintic drug resistance

Resistance of parasites to anthelmintic drugs is a growing global problem (Wanyangu *et al.*, 1996). Anthelmintic drug resistance is a real problem in the UK (Gordon *et al.*, 2012) and Australia (Brockwell *et al.*, 2014) and has also been reported in human in the Netherlands (Winkelhagen *et al.*, 2012). Anthelmintic resistance has been demonstrated using faecal egg count reduction (Coles *et al.*, 1992), copro-antigen reduction tests (Brockwell *et al.*, 2014) and egg hatch assay (Fairweather *et al.*, 2012). Demonstration of resistance to triclabendazole TCBZ (also the drug of choice in human fasciolosis) against immature and adult *Fasciola* indicates serious potential problems in controlling fasciolosis in future (Fairweather & Boray, 1999b). Burdens of 20–34 drug-resistant flukes were observed in cattle following treatment with triclabendazole in Australia (Brockwell *et al.*, 2014). However, studies have shown that, the anthelmintic drugs, nitroxylin and oxyclozanide were able to kill 100% and 99.6% of adult triclabendazole-resistant flukes respectively. Also albendazole caused up to 95% reduction in triclabendazole-resistant fluke egg counts while clorsulon showed 73.2% reduction (Coles & Stafford, 2001). This finding is consistent with those carried out recently that showed that the anthelmintic drugs, clorsulon and oxyclozanide were effective in removing adult triclabendazole-resistant flukes (Elliott *et al.*, 2015).

There are also reports of some isolates of *F. hepatica* being resistant to

albendazole in sheep (Sanabria *et al.*, 2013, Novobilsky *et al.*, 2012). A reduced efficacy of albendazole and oxclozanide against *F. gigantica* in naturally infected cattle has also been reported in Tanzania (Keyyu *et al.*, 2008). This could probably be the case with *F. gigantica* in Nigeria, hence further validation tests may be needed. There are currently few if any data on anthelmintic drug resistance in Nigerian cattle. However, a recent study in small ruminants suggests low resistance to ivermectin and levamisole with susceptibility to albendazole (Adediran and Uwalaka, 2015)

The incomplete elimination of infection leads to subclinical fasciolosis with continuous contamination of pasture especially in sheep (Ollerenshaw, 1971). An alternative strategy is to use a combination of drugs-synergistic drug usage (Fairweather & Boray, 1999b) and also treatment based on degree of infection (Malone & Craig, 1990) may be practical treatment strategies.

Human trematodiasis in Nigeria

Human fasciolosis has been reported from 51 countries over the last 25 years in the continents of Africa, America, Asia, Europe and Oceania (Mas-Coma *et al.*, 1999). Fasciolosis is among the most neglected tropical diseases (Mas-Coma *et al.*, 2009) with an estimated 180 million humans at risk of *Fasciola* speciesinfection worldwide (WHO, 1995), and with as many as 2.4 to 17 million humans which may be infected (Hopkins, 1992, Toledo *et al.*, 2012). Human infection with fasciolosis have been reported to occur from eating uncooked watercress derived from endemic areas where infected cattle range freely, and also probably from contaminated water (Stemmermann, 1953, Toledo *et al.*, 2012). Man is not a natural host of *F.gigantica* and most flukes derived from human beings are not fertile. As such coprological examination is not likely to be of value and only symptomatic cases would be discovered (Stemmermann, 1953). Human fasciolosis is determined by the presence of the intermediate snail host, domestic herbivorous animals, climatic conditions and the dietary habits of man (Chen and Mott, 1990). Mas-Coma *et al.*, (1999) reviewed the prevalence of *Fasciola* species reported in various parts of the world (Mas-Coma *et al.*, 1999).

The main methods of diagnosing human trematodiasis are direct parasitological

detection of fluke eggs in stool (Mas-Coma *et al.*, 2006) and other biofluids- (duodenal and biliary aspirates) and immune-diagnosis (indirect diagnosis). Other non-invasive diagnostic techniques such as radiology, ultrasound, computer tomography and magnetic resonance can also be used (Esteban *et al.*, 1998, Mas-Coma *et al.*, 2005, Keiser & Utzinger, 2009). In a recent review, stool and blood techniques have been reported to be improved for diagnosis of human fasciolosis and during surveys. However the author also identified difficulties of diagnosing fascioliasis in humans due to different infection phases and parasite migration capacities, clinical heterogeneity, immunological complexity, different epidemiological situations and transmission patterns (Mas-coma *et al.*, 2014).

Human fasciolosis have been reported in Africa involving both species of *Fasciola* (Mas-Coma *et al.*, 1999). There are hardly any studies targeted at detecting the zoonotic effect of fasciolosis in Nigeria. In a study there was a report of the positive detection of *Fasciola* species in HIV-infected human subjects in Nigeria though at low prevalence rate of 1% (Abaver *et al.*, 2012). This suggests that human infection may be significant although further research on risk factors as well as possible routes of transmission needs to be carried out.

Human cases of dicrocoeliasis are rare and often occur by accidental ingestion of infected ants on unwashed vegetables or by drinking contaminated water (Haridy *et al.*, 2003). Human cases of dicrocoeliasis have been reported in Nigeria (Roche, 1948, Samaila *et al.*, 2009), Czechoslovakia (Ondriska *et al.*, 1989), Egypt (Massoud *et al.*, 2003), Turkey (Cengiz *et al.*, 2010) and Kyrgyzstan (Jeandron *et al.*, 2011). Spurious infection with *D. hospes* has also been reported in Ghana due to accidental ingestion of infected animal liver (Wolfe, 1966). The subclinical form of the disease, which is most common, is characterized by cholangitis and adenomatous proliferation of the bile duct (Cabeza-Barrera *et al.*, 2011). Other signs are constipation, diarrhoea, vomiting and abdominal pain (Ondriska *et al.*, 1989). Human dicrocoeliasis has been reported in a 7-year old Nigerian child of a nomadic pastoralist showing clinical signs of fever, jaundice and anterior subcutaneous abdominal mass (Samaila *et al.*, 2009).

The amphistome species reported in man is *Gastrodiscoides hominis* and is widely distributed in Asia. It is located in the caecum and colon, with pigs being the main animal reservoir (Dutt & Srivastava, 1972) and has been reported in Nigeria in a malnourished child (Dada-Adegbola *et al.*, 2004).

Although *S. bovis* is primarily infects ruminant, it has been isolated in man in various parts of Africa (Raper, 1951, Chungue *et al.*, 1986, Santoro, 1988, Kinoti & Mumo, 1988). Moreover, the mesenteries of cattle, which may be infected with *S. bovis*, are usually sold at the local markets in Africa as edible tripe thus making it public health risk (Kamanja *et al.*, 2011). Hybridization between *S. bovis* and *S. haematobium* (cattle and human infection) in Senegal has been reported with an impending risk of the emergence of a new disease (Huyse *et al.*, 2009).

Several drugs for the effective treatment of human fasciolosis are available. These include dihydroemetine-emetine derivative, bithionol, praziquantel and triclabendazole (effective against both acute and chronic fasciolosis). These are currently the drugs of choice for human fasciolosis caused by both *F. hepatica* and *F. gigantica* (Esteban *et al.*, 1998, Savioli *et al.*, 1999). Praziquantel has also been used in treatment of human dicrocoeliasis (Massoud *et al.*, 2003). Mebendazole was effective in treatment of the human amphistomosis (Dada-Adegbola *et al.*, 2004).

The prevention of human trematode infections may be achieved by strict control of water cress and other metacercariae carrying aquatic plants for human consumption especially in endemic zone (Mas-Coma *et al.*, 2005). Drinking water must be boiled or purified. Integrated control approaches and inter-sectoral collaboration between public health and veterinary medicine has also been suggested for control (Keiser & Utzinger, 2009).

Conclusions and recommendations.

Trematode infections are a significant limiting factor in livestock production; therefore development of sustainable strategies for their control is a priority. In order to develop sustainable control, gap in knowledge must be identified to guide research projects. The outcome of such research would enhance proper allocation

of funds for disease control and policy formulation. In addition, it is also important to carry out detailed study on the overall economic losses due from trematode infections in order to design and implement appropriate systematic disease prevention and control methods.

The prevalence rates of trematodes reported across the various abattoirs in Nigeria are an indication that trematode infection poses widespread risk to livestock and possibly humans. However, it is worthy of note that neither oxcylozanide nor triclabendazole, which are the 2 drugs of choice for mixed and human *Fasciola* infection respectively is currently not available for use in Nigeria. Availability of these two drugs could be helpful in reducing diseases occurrence. These drugs could be made available by formulating favourable policies that ensure the drug retailers have basic training to identify and stock the appropriate drugs of choice and informing livestock farmers on rationale for use (example is information on effectiveness of triclabendazole against both mature and immature flukes). The gap in technical knowledge needed by drug retailers for dispensing drugs has been identified in a previous study (Bett *et al.*, 2004) and veterinarians have a huge responsibility in advising/training these retailers on the appropriate drugs to stock based on the diseases prevalent to different localities.

There are hardly any studies targeted at detecting the zoonotic effect of fasciolosis infections in Nigeria. Although a few studies exist on other trematodes in Nigeria, these are often case reports. Further research on burden, risk factors as well as possible routes of transmission of trematode infection to human needs to be carried out.

Molecular studies on trematodes in different species of livestock including those targeted at understanding anthelmintic drug resistance should also be carried out across Nigeria. These studies would be useful in providing more data on the diversity of these important trematodes.

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Statement of interest

None

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Figure 1: Geographical distribution of bovine fasciolosis across different states of Nigeria (1980–2016) from published prevalence (%) data based on abattoir records, liver and coprological examination. States with 0% have no available data as at time of review.

